WO 2005/103083 PCT/IB2005/002476

Figure 1a

Variable Heavy Chain DNA

3077 VH1B (SEQ ID NO: 1):

- (1) CAGGTGCAAT TGGTTCAGAG CGGCGCGGAA GTGAAAAAAC CGGGCGCGAG
- (51) CGTGAAAGTG AGCTGCAAAG CCTCCGGATA TACCTTTACT TCTTATTCTA
- (101) TTAATTGGGT CCGCCAAGCC CCTGGGCAGG GTCTCGAGTG GATGGGCTAT
- (151) ATCGATCCGA ATCGTGGCAA TACGAATTAC GCGCAGAAGT TTCAGGGCCG
- (201) GGTGACCATG ACCCGTGATA CCAGCATTAG CACCGCGTAT ATGGAACTGA
- (251) GCAGCCTGCG TAGCGAAGAT ACGGCCGTGT ATTATTGCGC GCGTGAGTAT
- (301) ATTTATTTTA TTCATGGTAT GCTTGATTTT TGGGGCCAAG GCACCCTGGT
- (351) GACGGTTAGC TCA

3079_VH3 (SEQ ID NO: 2):

- (1) CAGGTGCAAT TGGTGGAAAG CGGCGGCGGC CTGGTGCAAC CGGGCGGCAG
- (51) CCTGCGTCTG AGCTGCGCGG CCTCCGGATT TACCTTTTCT AATTATGGTA
- (101) TGCATTGGGT GCGCCAAGCC CCTGGGAAGG GTCTCGAGTG GGTGAGCAAT
- (151) ATCCGTTCTG ATGGTAGCTG GACCTATTAT GCGGATAGCG TGAAAGGCCG
- (201) TTTTACCATT TCACGTGATA ATTCGAAAAA CACCCTGTAT CTGCAAATGA
- (251) ACAGCCTGCG TGCGGAAGAT ACGGCCGTGT ATTATTGCGC GCGTCGTTAT
- (301) TGGTCTAAGT CTCATGCTTC TGTTACTGAT TATTGGGGCC AAGGCACCCT
- (351) GGTGACGGTT AGCTCA

3080 VH3 (SEQ ID NO: 3):

- (1) CAGGTGCAAT TGGTGGAAAG CGGCGGCGGC CTGGTGCAAC CGGGCGGCAG
- (51) CCTGCGTCTG AGCTGCGCGG CCTCCGGATT TACCTTTTCT TCTTATGGTA
- (101) TGCATTGGGT GCGCCAAGCC CCTGGGAAGG GTCTCGAGTG GGTGAGCAAT
- (151) ATCTATTCTG ATGGTAGCAA TACCTTTTAT GCGGATAGCG TGAAAGGCCG
- (201) TTTTACCATT TCACGTGATA ATTCGAAAAA CACCCTGTAT CTGCAAATGA
- (251) ACAGCCTGCG TGCGGAAGAT ACGGCCGTGT ATTATTGCGC GCGTAATATG
- (301) TATCGTTGGC CTTTTCATTA TTTTTTTGAT TATTGGGGCC AAGGCACCCT
- ·(351) GGTGACGGTT AGCTCA

3100 VH 3 (SEQ ID NO: 4):

- (1) CAGGTGCAAT TGGTGGAAAG CGGCGGCGC CTGGTGCAAC CGGGCGGCAG
- (51) CCTGCGTCTG AGCTGCGCGG CCTCCGGATT TACCTTTTCT TCTAATGGTA
- (101) TGTCTTGGGT GCGCCAAGCC CCTGGGAAGG GTCTCGAGTG GGTGAGCAAT
- (151) ATCTCTTATC TTTCTAGCTC TACCTATTAT GCGGATAGCG TGAAAGGCCG
- (201) TTTTACCATT TCACGTGATA ATTCGAAAAA CACCCTGTAT CTGCAAATGA
- (251) ACAGCCTGCG TGCGGAAGAT ACGGCCGTGT ATTATTGCGC GCGTTTTTAT
- (301) GGTTATTTTA ATTATGCTGA TGTTTGGGGC CAAGGCACCC TGGTGACGGT
- (351) TAGCTCA

3077 1 VH1B (SEQ ID NO: 31):

- (1) CAGGTGCAAT TAGTCCAAAG TGGTGCGGAA GTGAAAAAAC CGGGCGCGAG
- (51) CGTGAAAGTG AGCTGCAAAG CCTCCGGATA TACCTTTACT TCTTATTCTA

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(101) TTAATTGGGT	CCGCCAAGCC	CCTGGGCAGG	${\tt GTCTCGAGTG}$	GATGGGCTAT
(151) ATCGATCCGA	ATCGTGGCAA	TACGAATTAC	$\tt GCGCAGAAGT$	TTCAGGGCCG
(201) GGTGACCATG	ACCCGTGATA	CCAGCATTAG	CACCGCGTAT	ATGGAACTGA
(251) GCAGCCTGCG	TAGCGAAGAT	ACGGCCGTGT	ATTATTGCGC	GCGTGAGTAT
(301) ATTTATTTTA	TTCATGGTAT	GCTTGATTTT	TGGGGCCAAG	GCACCCTGGT
(351) GACGGTTAGC	TCA			

Figure 1b

Variable Heavy Chain Peptide

(CDR Regions in Bold)

3077 VH1B (SEQ ID NO: 5):

- (1) QVQLVQSGAE VKKPGASVKV SCKAS**GYTFT SYSIN**WVRQA PGQGLEWMG**Y**
- (51) IDPNRGNTNY AQKFQGRVTM TRDTSISTAY MELSSLRSED TAVYYCAREY
- (101) IYFIHGMLDF WGQGTLVTVS S

3079 VH3 (SEQ ID NO: 6):

- (1) QVQLVESGGG LVQPGGSLRL SCAASGFTFS NYGMHWVRQA PGKGLEWVSN
- (51) IRSDGSWTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARRY
- (101) WSKSHASVTD YWGQGTLVTV SS

3080_VH3 (SEQ ID NO: 7):

- (1) QVQLVESGGG LVQPGGSLRL SCAASGFTFS SYGMHWVRQA PGKGLEWVSN
- (51) IYSDGSNTFY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARNM
- (101) YRWPFHYFFD YWGQGTLVTV SS

3100_VH 3 (SEQ ID NO: 8):

- (1) QVQLVESGGG LVQPGGSLRL SCAASGFTFS SNGMSWVRQA PGKGLEWVSN
- (51) ISYLSSTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARFY
- (101) GYFNYADVWG QGTLVTVSS

Figure 2a

Variable Light Chain DNA

3077_Vk kappa 2 (SEQ ID NO: 9):

(1)	GATATCGTGA	TGACCCAGAG	CCCACTGAGC	CTGCCAGTGA	CTCCGGGCGA
(51)	GCCTGCGAGC	ATTAGCTGCA	GAAGCAGCCA	AAGCCTGCTT	TTTATTGATG
(101)	GCAATAATTA	TCTGAATTGG	TACCTTCAAA	AACCAGGTCA	AAGCCCGCAG
(151)	CTATTAATTT	ATCTTGGTTC	TAATCGTGCC	AGTGGGGTCC	CGGATCGTTT
	TAGCGGCTCT				
	AAGCTGAAGA				
	GCTACCTTTG				

3079_Vk kappa 1 (SEQ ID NO: 10):

(1)	GATATCCAGA	TGACCCAGAG	CCCGTCTAGC	CTGAGCGCGA	GCGTGGGTGA
(51)	TCGTGTGACC	ATTACCTGCA	GAGCGAGCCA	GGATATTTCT	GCTTTTCTGA
(101)	ATTGGTACCA	GCAGAAACCA	GGTAAAGCAC	CGAAACTATT	AATTTATAAG
(151)	GTTTCTAATT	TGCAAAGCGG	GGTCCCGTCC	CGTTTTAGCG	GCTCTGGATC
(201)	CGGCACTGAT	TTTACCCTGA	CCATTAGCAG	CCTGCAACCT	GAAGACTTTG
(251)	CGACTTATTA	TTGCCAGCAG	GCTTATTCTG	GTTCTATTAC	CTTTGGCCAG
	GGTACGAAAG				

3080 VI lambda 3 (SEQ ID NO: 11):

(1)	GATATCGAAC	TGACCCAGCC	GCCTTCAGTG	AGCGTTGCAC	CAGGTCAGAC
(51)	CGCGCGTATC	TCGTGTAGCG	GCGATAATAT	TGGTAATAAG	TATGTTTCTT
(101)	GGTACCAGCA	GAAACCCGGG	CAGGCGCCAG	TTGTTGTGAT	TTATGGTGAT
	AATAATCGTC				
	CAACACCGCG				
	ATTATTATTG			ATTTTGTGTT	TGGCGGCGGC
(301)	ACGAAGTTAA	CCGTTCTTGG	CCAG		

3100_Vl lambda 3 (SEQ ID NO: 12):

(1)	GATATCGAAC	TGACCCAGCC	GCCTTCAGTG	AGCGTTGCAC	CAGGTCAGAC
(51)	CGCGCGTATC	TCGTGTAGCG	GCGATAATAT	TGGTCATTAT	TATGCTTCTT
(101)	GGTACCAGCA	GAAACCCGGG	CAGGCGCCAG	TTCTTGTGAT	TTATCGTGAT
				TTTAGCGGAT	
				TCAGGCGGAA	
(251)	ATTATTATTG	CCAGTCTTAT	GATTATCTTC	ATGATTTTGT	GTTTGGCGGC
(301)	GGCACGAAGT	TAACCGTTCT	TGGCCAG		

Figure 2b

Variable Light Chain Peptide

(CDR Regions in Bold)

3077_Vk kappa 2 (SEQ ID NO: 13):

- (1) DIVMTQSPLS LPVTPGEPAS ISCRSSQSLL FIDGNNYLNW YLQKPGQSPQ
- (51) LLIYLGSNRA SGVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYCQQYSSKS
- (101) ATFGQGTKVE IKRT

3079 Vk kappa 1 (SEQ ID NO: 14):

- (1) DIQMTQSPSS LSASVGDRVT ITCRASQDIS AFLNWYQQKP GKAPKLLIYK
- (51) VSNLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ AYSGSITFGQ
- (101) GTKVEIKRT

3080_VI lambda 3 (SEQ ID NO: 15):

- (1) DIELTQPPSV SVAPGQTARI SCSGDNIGNK YVSWYQQKPG QAPVVVIYGD
- (51) NNRPSGIPER FSGSNSGNTA TLTISGTQAE DEADYYCSSY DSSYFVFGGG
- (101) TKLTVLGQ

3100_Vl lambda 3 (SEQ ID NO: 16):

- (1) DIELTOPPSV SVAPGOTARI SCSGDNIGHY YASWYQQKPG QAPVLVIYRD
- (51) NDRPSGIPER FSGSNSGNTA TLTISGTQAE DEADYYCQSY DYLHDFVFGG
- (101) GTKLTVLGQ

Variable Heavy Chain Consensus Sequences

(CDR Regions in Bold)

VH1B Consensus (SEQ ID NO: 17):

- (1) QVQLVQSGAE VKKPGASVKV SCKAS**GYTFT SYYMH**WVRQA PGQGLEWMG**W**
- (51) INPNSGGTNY AQKFQGRVTM TRDTSISTAY MELSSLRSED TAVYYCARWG
- (101) GDGFYAMDYW GQGTLVTVSS

VH3 Consensus (SEQ ID NO: 18):

- (1) QVQLVESGGG LVQPGGSLRL SCAAS**GFTFS SYAMS**WVRQA PGKGLEWVS**A**
- (51) ISGSGGSTYY ADSVKGRFTI SRDNSKNTLY LQMNSLRAED TAVYYCARWG
- (101) GDGFYAMDYW GQGTLVTVS S

Variable Light Chain Consensus Sequences

(CDR Regions in Bold)

VL λ3 Consensus (SEQ ID NO: 19):

- (1) SYELTOPPSV SVAPGOTARI SCSGDALGDK YASWYQQKPG QAPVLVIYDD
- (51) SDRPSGIPER FSGSNSGNTA TLTISGTQAE DEADYYCQQH YTTPPVFGGG
- (101) TKLTVLG

VL k1 Consensus (SEQ ID NO: 20):

- (1) DIQMTQSPSS LSASVGDRVT ITCRASQGIS SYLAWYQQKP GKAPKLLIYA
- (51) ASSLQSGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQQ HYTTPPTFGQ
- (101) GTKVEIKR

VL k2 Consensus (SEQ ID NO: 21):

- (1) DIVMTQSPLS LPVTPGEPAS ISCRSSQSLL HSNGYNYLDW YLQKPGQSPQ
- (51) LLIY**LGSNRA S**GVPDRFSGS GSGTDFTLKI SRVEAEDVGV YYC**QQHYTTP**
- (101) PTFGQGTKVE IKR

Peptide Sequence of CD38

(SEQ ID NO: 22):

mancefspvs gdkpccrlsr raqlclgvsi lvlilvvvla vvvprwrqqw sgpgttkrfp
etvlarcvky teihpemrhv dcqsvwdafk gafiskhpcn iteedyqplm klgtqtvpcn
killwsrikd lahqftqvqr dmftledtll gyladdltwc gefntskiny qscpdwrkdc
snnpvsvfwk tvsrrfaeaa cdvvhvmlng srskifdkns tfgsvevhnl qpekvqtlea
wvihggreds rdlcqdptik elesiiskrn iqfsckniyr pdkflqcvkn pedssctsei

Nucleotide Sequence of Chimeric OKT10

Heavy Chain (SEQ ID NO: 23):

caggtggaat tggtggaatc tggaggatcc ctgaaactct cctgtgcagc ctcaggattc gattttagta gatcctggat gaattgggtc cggcaggctc caggaaaagg gctagaatgg attggagaaa ttaatccaga tagcagtacg ataaactata cgacatctct aaaggataaa ttcatcatct ccagagacaa cgccaaaaat acgctgtacc tgcaaatgac caaagtgaga tctgaggaca cagcccttta ttactgtgca agatatggta actggtttcc ttattggggc caagggactc tggtcactgt cagctcagcc tccaccaagg gtccatcggt cttccccctg gcaccetect ccaagageae etetggggge acageggeee tgggetgeet ggtcaaggae tacttccccg aaccggtgac ggtgtcgtgg aactcaggcg ccctgaccag cggcgtgcac accttcccgg ctgtcctaca gtcctcagga ctctactccc tcagcagcgt ggtgaccgtg ccctccagca gcttgggcac ccagacctac atctgcaacg tgaatcacaa gcccagcaac accaaggtgg acaagaaagt tgagcccaaa tcttgtgaca aaactcacac atgcccaccg tgcccagcac ctgaactcct ggggggaccg tcagtcttcc tcttcccccc aaaacccaag gacaccetea tgateteceg gacceetgag gteacatgeg tggtggtgga egtgageeae gaagaccctg aggtcaagtt caactggtac gtggacggcg tggaggtgca taatgccaag acaaagccgc gggaggagca gtacaacagc acgtaccggg tggtcagcgt cctcaccgtc ctgcaccagg actggctgaa tggcaaggag tacaagtgca aggtctccaa caaagccctc ccagccccca tcgagaaaac catctccaaa gccaaagggc agccccgaga accacaggtg tacaccetge ecceateceg ggatgagetg accaagaace aggteageet gacetgeetg gtcaaagget tetateecag egacategee gtggagtggg agageaatgg geageeggag aacaactaca agaccacgcc tcccgtgctg gactccgacg gctccttctt cctctacagc aagctcaccg tggacaagag caggtggcag caggggaacg tcttctcatg ctccgtgatg catgaggete tgeacaacea etacaegeag aagageetet eeetgtetee gggtaaa

Light Chain (SEQ ID NO: 24):

gatatectga tgaeccagte teaaaaaate atgeecacat cagtgggaga cagggteage gteacetgea aggeeagtea aaatgtggat actaatgtag eetggtatea acagaaacca

ggacagtctc	ctaaagcact	gatttactcg	gcatcctacc	gatacagtgg	agtccctgat
cgcttcacag	gcagtggatc	tgggacagat	ttcactctca	ccatcaccaa	tgtgcagtct
gaggacttgg	cagagtattt	ctgtcagcaa	tatgacagct	atcctctcac	gttcggtgct
gggaccaagc	tggacctgaa	acgtacggtg	gctgcaccat	ctgtcttcat	cttcccgcca
tctgatgagc	agttgaaatc	tggaactgcc	tctgttgtgt	gcctgctgaa	taacttctat
cccagagagg	ccaaagtaca	gtggaaggtg	gataacgccc	tccaatcggg	taactcccag
gagagtgtca	cagagcagga	cagcaaggac	agcacctaca	gcctcagcag	caccctgacg
ctgagcaaag	cagactacga	gaaacacaaa	gtctacgcct	gcgaagtcac	ccatcagggc
ctgagctcgc	ccgtcacaaa	gagcttcaac	aggggagagt	gt	

Fig.7: Schematic Overview of Epitopes

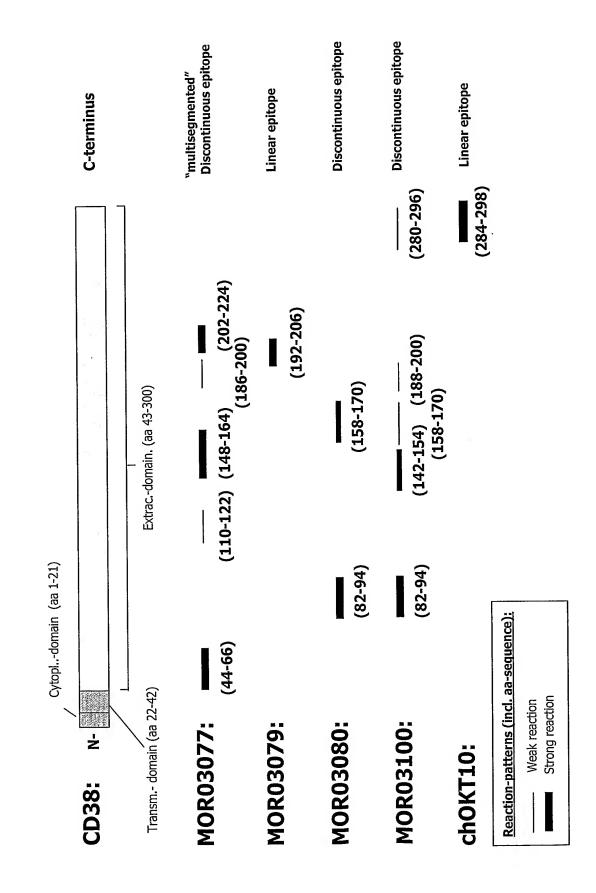


Figure 8: DNA sequence of pMOPRH®_h_IgG1_1

	Styl
601	TCGCTATTAC CATGGTGATG CGGTTTTGGC AGTACATCAA TGGGCGTGGA
	AGCGATAATG GTACCACTAC GCCAAAACCG TCATGTAGTT ACCCGCACCT
	AatII ~~~~~~
651	TAGCGGTTTG ACTCACGGGG ATTTCCAAGT CTCCACCCCA TTGACGTCAA
	ATCGCCAAAC TGAGTGCCCC TAAAGGTTCA GAGGTGGGGT AACTGCAGTT
701	TGGGAGTTTG TTTTGGCACC AAAATCAACG GGACTTTCCA AAATGTCGTA
	ACCCTCAAAC AAAACCGTGG TTTTAGTTGC CCTGAAAGGT TTTACAGCAT
751	ACAACTCCGC CCCATTGACG CAAATGGGCG GTAGGCGTGT ACGGTGGGAG
	TGTTGAGGCG GGGTAACTGC GTTTACCCGC CATCCGCACA TGCCACCCTC
801	GTCTATATAA GCAGAGCTCT CTGGCTAACT AGAGAACCCA CTGCTTACTG
	CAGATATATT CGTCTCGAGA GACCGATTGA TCTCTTGGGT GACGAATGAC
	pMORPH®_Ig_FOR 100.0% NheI
851	GCTTATCGAA ATTAATACGA CTCACTATAG GGAGACCCAA GCTGGCTAGC
	CGAATAGCTT TAATTATGCT GAGTGATATC CCTCTGGGTT CGACCGATCG
	M K H L W F F L L L V A A P R
901	GCCACCATGA AACACCTGTG GTTCTTCCTC CTGCTGGTGG CAGCTCCCAG
901	CGGTGGTACT TTGTGGACAC CAAGAAGGAG GACGACCACC GTCGAGGGTC
	EcoRI BlpI
StyI	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~
	A S T
•	. W V L S O V E F C R R L A Q
951	ATGGGTCCTG TCCCAGGTGG AATTCTGCAG GCGGTTAGCT CAGCCTCCAC
	TACCCAGGAC AGGGTCCACC TTAAGACGTC CGCCAATCGA GTCGGAGGTG
	StyI BbsI
	· K G P S V F P L A P S S K S T S G
1001	CAAGGGTCCA TCGGTCTTCC CCCTGGCACC CTCCTCCAAG AGCACCTCTG
1001	GTTCCCAGGT AGCCAGAAGG GGGACCGTGG GAGGAGGTTC TCGTGGAGAC
	· G T A A L G C L V K D Y F P E P
1051	GGGGCACAGC GGCCCTGGGC TGCCTGGTCA AGGACTACTT CCCCGAACCG
	CCCCGTGTCG CCGGGACCCG ACGGACCAGT TCCTGATGAA GGGGCTTGGC

	V T V S W N S G A L T S G V H T F
1101	GTGACGGTGT CGTGGAACTC AGGCGCCCTG ACCAGCGGCG TGCACACCTT CACTGCCACA GCACCTTGAG TCCGCGGGAC TGGTCGCCGC ACGTGTGGAA
	PAVLQSSGLYSCVVT
1151	CCCGGCTGTC CTACAGTCCT CAGGACTCTA CTCCCTCAGC AGCGTGGTGA GGGCCGACAG GATGTCAGGA GTCCTGAGAT GAGGGAGTCG TCGCACCACT
1201	· V P S S S L G T Q T Y I C N V N CCGTGCCCTC CAGCAGCTTG GGCACCCAGA CCTACATCTG CAACGTGAAT GGCACGGGAG GTCGTCGAAC CCGTGGGTCT GGATGTAGAC GTTGCACTTA
	StyI
	H K P S N T K V D K K V E P K S C
1251	CACAAGCCCA GCAACACCAA GGTGGACAAG AAAGTTGAGC CCAAATCTTG GTGTTCGGGT CGTTGTGGTT CCACCTGTTC TTTCAACTCG GGTTTAGAAC
	· D K T H T C P P C P A P E L L G G
1301	TGACAAAACT CACACATGCC CACCGTGCCC AGCACCTGAA CTCCTGGGGG ACTGTTTTGA GTGTGTACGG GTGGCACGGG TCGTGGACTT GAGGACCCCC
	BbsI StyI
1351	\cdot P S V F L F P P K P K D T L M I GACCGTCAGT CTTCCTCTTC CCCCCAAAAC CCAAGGACAC CCTCATGATC CTGGCAGTCA GAAGGAGAAG GGGGGTTTTG GGTTCCTGTG GGAGTACTAG
	BbsI
	S R T P E V T C V V V D V S H E D
1401	TCCCGGACCC CTGAGGTCAC ATGCGTGGTG GTGGACGTGA GCCACGAAGA AGGGCCTGGG GACTCCAGTG TACGCACCAC CACCTGCACT CGGTGCTTCT
	BbsI ~
	- P E V K F N W Y V D G V E V H N A
1451	CCCTGAGGTC AAGTTCAACT GGTACGTGGA CGGCGTGGAG GTGCATAATG GGGACTCCAG TTCAAGTTGA CCATGCACCT GCCGCACCTC CACGTATTAC
1501	· K T K P R E E Q Y N S T Y R V V CCAAGACAAA GCCGCGGAG GAGCAGTACA ACAGCACGTA CCGGGTGGTC GGTTCTGTTT CGGCGCCCTC CTCGTCATGT TGTCGTGCAT GGCCCACCAG
	GGIICIGIII CGGCGCCCIC CICGICAIGI IGICGIGCAI GGGCCAICCAIC
	S V L T V L H Q D W L N G K E Y K
1551	AGCGTCCTCA CCGTCCTGCA CCAGGACTGG CTGAATGGCA AGGAGTACAA TCGCAGGAGT GGCAGGACGT GGTCCTGACC GACTTACCGT TCCTCATGTT
	· C K V S N K A L P A P I E K T I S
1601	GTGCAAGGTC TCCAACAAAG CCCTCCCAGC CCCCATCGAG AAAACCATCT CACGTTCCAG AGGTTGTTTC GGGAGGGTCG GGGGTAGCTC TTTTGGTAGA

	BsrGI	
1651	· K A K G Q P R E P Q V Y T L P P CCAAAGCCAA AGGGCAGCCC CGAGAACCAC AGGTGTACAC CCTGCCCCCA GGTTTCGGTT TCCCGTCGGG GCTCTTGGTG TCCACATGTG GGACGGGGGT	
	S R D E L T K N Q V S L T C L V K	
1701	TCCCGGGATG AGCTGACCAA GAACCAGGTC AGCCTGACCT GCCTGGTCAA AGGGCCCTAC TCGACTGGTT CTTGGTCCAG TCGGACTGGA CGGACCAGTT	
	GFYPSDIAVEWESNGQP	
1751	AGGCTTCTAT CCCAGCGACA TCGCCGTGGA GTGGGAGAGC AATGGGCAGC TCCGAAGATA GGGTCGCTGT AGCGGCACCT CACCCTCTCG TTACCCCGTCG	
1801	· E N N Y K T T P P V L D S D G S CGGAGAACAA CTACAAGACC ACGCCTCCCG TGCTGGACTC CGACGGCTCC GCCTCTTGTT GATGTTCTGG TGCGGAGGGC ACGACCTGAG GCTGCCGAGG	
	F F L Y S K L T V D K S R W Q Q G	
1851	TTCTTCCTCT ACAGCAAGCT CACCGTGGAC AAGAGCAGGT GGCAGCAGGG AAGAAGGAGA TGTCGTTCGA GTGGCACCTG TTCTCGTCCA CCGTCGTCCC	
	BbsI NsiI	
	· N V F S C S V M H E A L H N H Y T	
1901	GAACGTCTTC TCATGCTCCG TGATGCATGA GGCTCTGCAC AACCACTACA CTTGCAGAAG AGTACGAGGC ACTACGTACT CCGAGACGTG TTGGTGATGT	
	SapI PmeI	
1951	• Q K S L S L S P G K * CGCAGAAGAG CCTCTCCCTG TCTCCGGGTA AATGAGGGCC CGTTTAAACC GCGTCTTCTC GGAGAGGGAC AGAGGCCCAT TTACTCCCGG GCAAATTTGG	
2001	CGCTGATCAG CCTCGACTGT GCCTTCTAGT TGCCAGCCAT CTGTTGTTTG GCGACTAGTC GGAGCTGACA CGGAAGATCA ACGGTCGGTA GACAACAAAC	
2051	pMORPH [®] _Ig_REV 100.0% CCCCTCCCC GTGCCTTCCT TGACCCTGGA AGGTGCCACT CCCACTGTCC CGGGAGGGG CACGGAGGA ACTGGGACCT TCCACGGTGA GGGTGACAGG	

Figure 9: DNA Sequence of Ig kappa light chain expression vector pMORPH®_h_Igk_1

		styI			
601	ጥርርርም <u>ል</u> ጥጥልር	-~~~~ Catggtgatg	CGGTTTTGGC	AGTACATCAA	TGGGCGTGGA
90T	AGCGATAATG	GTACCACTAC	GCCAAAACCG	TCATGTAGTT	ACCCGCACCT
651				CTCCACCCCA	
	ATCGCCAAAC	TGAGTGCCCC	TAAAGGTTCA	GAGGTGGGGT	AACTGCAGTT
701	тасалатта	TTTTGGCACC	AAAATCAACG	GGACTTTCCA	AAATGTCGTA
701				CCTGAAAGGT	
751				GTAGGCGTGT	
	TGTTGAGGCG	GGGTAACTGC	GTTTACCCGC	CATCCGCACA	TGCCACCCTC
801	СТСТАТАТАА	GCAGAGCTCT	CTGGCTAACT	AGAGAACCCA	CTGCTTACTG
001				TCTCTTGGGT	
			_IgFOR 1009		NheI
0.51			 	=== GGAGACCCAA	GCTGGCTAGC
851				CCTCTGGGTT	
	COLLILIZACE				
+1	M	V L Q T	Q V F	I S L	r r M 1
	StyI				
901	~~~~~	ጥ ረጥጥረር እር እር	CCAGGTCTTC	ATTTCTCTGT	TGCTCTGGAT
901	CGGTGGTACC	ACAACGTCTG	GGTCCAGAAG	TAAAGAGACA	ACGAGACCTA
			BbsI		
			~~~~~		
	s G A	Y G D	ı v m ı	KRT	V A A
+1.	S G A	Eco		BsiWI	•
		~~~	~~~	~~~~~	
951				TAAACGTACG	
	GAGACCACGG	ATGCCCCTAT	' AGCACTACTA	ATTTGCATGC	CACCGACGTG
. 1	PSVF	TFP	P S D	E O L K	SGT
1001				AGCAGTTGAA	
2001				TCGTCAACTT	
	BbsI				
	~~~~	~~			

16/24

- +1 A S V V C L L N N F Y P R E A K V

  1051 GCCTCTGTTG TGTGCCTGCT GAATAACTTC TATCCCAGAG AGGCCAAAGT
  CGGAGACAAC ACACGGACGA CTTATTGAAG ATAGGGTCTC TCCGGTTTCA
- +1 Q W K V D N A L Q S G N S Q E S 1101 ACAGTGGAAG GTGGATAACG CCCTCCAATC GGGTAACTCC CAGGAGAGTG TGTCACCTTC CACCTATTGC GGGAGGTTAG CCCATTGAGG GTCCTCTCAC
- +1 V T E Q D S K D S T Y S L S S T L

  1151 TCACAGAGCA GGACAGCAAG GACAGCACCT ACAGCCTCAG CAGCACCCTG

  AGTGTCTCGT CCTGTCGTTC CTGTCGTGGA TGTCGGAGTC GTCGTGGGAC
  - +1 T L S K A D Y E K H K V Y A C E V BlpI
- 1201 ACGCTGAGCA AAGCAGACTA CGAGAAACAC AAAGTCTACG CCTGCGAAGT TGCGACTCGT TTCGTCTGAT GCTCTTTGTG TTTCAGATGC GGACGCTTCA
- +1 T H Q G L S S P V T K S F N R G

  1251 CACCCATCAG GGCCTGAGCT CGCCCGTCAC AAAGAGCTTC AACAGGGGAG
  GTGGGTAGTC CCGGACTCGA GCGGGCAGTG TTTCTCGAAG TTGTCCCCTC
  - +1 E C *

~~~~~~

PmeI pMORPH Ig\_REV 100%

- 1301 AGTGTTAGGG GCCCGTTTAA ACCCGCTGAT CAGCCTCGAC TGTGCCTTCT TCACAATCCC CGGGCAAATT TGGGCGACTA GTCGGAGCTG ACACGGAAGA
- 1351 AGTTGCCAGC CATCTGTTGT TTGCCCCTCC CCCGTGCCTT CCTTGACCCT
 TCAACGGTCG GTAGACAACA AACGGGGAGG GGGCACGGAA GGAACTGGGA

17/24

Figure 10: DNA Sequence of HuCAL $^{\rm B}$ Ig lambda light chain vector pMORPH $^{\rm B}_{\rm L}$ Lg $^{\rm L}$

| | | StyI | | | |
|------|-------------------|---|--|--------------------------|------------------------|
| | ~- | ~~~~~ | ecomposition of the control of the c | 7 CW7 C7 WC7 7 | madadamaa. |
| 601 | | | | AGTACATCAA
TCATGTAGTT | |
| | | | | | |
| 651 | TAGCGGTTTG | ACTCACGGGG | ATTTCCAAGT | CTCCACCCA | TTGACGTCAA |
| | ATCGCCAAAC | TGAGTGCCCC | TAAAGGTTCA | GAGGTGGGGT | AACIGCAGIII |
| 701 | TGGGAGTTTG | TTTTGGCACC | AAAATCAACG | GGACTTTCCA | AAATGTCGTA |
| | ACCCTCAAAC | AAAACCGTGG | TTTTAGTTGC | CCTGAAAGGT | TTTACAGCAT |
| 251 | * C * * C C C C C | CCCN TTCN CC | CNNTCCCCC | GTAGGCGTGT | ACGGTGGGAG |
| 751 | TGTTGAGGCG | GGGTAACTGC | GTTTACCCGC | CATCCGCACA | TGCCACCCTC |
| | | | | | |
| 801 | | | | AGAGAACCCA
TCTCTTGGGT | |
| | CAGATATATT | CGTCTCGAGA | GACCGATTGA | TCTCTTGGGT | GACGAATGAC |
| | | pM_Ig_ | FOR 100.0% | | NheI |
| | | | ====================================== | | ~~~~~ |
| 851 | GCTTATCGAA | . ATTAATACGA
TAATTATGCT | GAGTGATATC | GGAGACCCAA
CCTCTGGGTT | CGACCGATCG |
| | CGAAIACCII | 111111111111111111111111111111111111111 | | | |
| +1 | StyI | A W A L | LLL | T L L | T Q G T |
| 901 | CCCACCATGG | | · GOTGOTCOTO | ACCCTCCTCA | CTCAGGGCAC |
| 901 | | | | TGGGAGGAGT | |
| +2 | | | | | L G Q |
| +1 | g s W | | V M H E | | StyI |
| | BamHI | EcoRV | | HpaI
~~~~~ | 2071 |
| 951 | AGGATCCTGG | | | AGTTAACCGT | |
| | TCCTAGGACC | CGACTATAGO | ACTACGTGCT | TCAATTGGCA | GGATCCAGTC |
| +2 | рка | APSV | TLF | PPS | SEEL |
| 72 | styI | | | | |
| | ~~~~ | | | | |
| 1001 | | | | CCGCCCTCCT GGCGGGAGGA | |
| | GGGTTCCCAC | , 00000110001 | . 010 | | |
| +2 | | | | I S D | F Y P |
| 1051 | TCAAGCCAAC | AAGGCCACAC | TGGTGTGTCT | CATAAGTGAC
GTATTCACTG | TTCTACCCGC AAGATCCCCC |
| | AGTICGGTIC | 2 TICCGGIGIC | ACCHCHCHCH | TATICACIO | 11101110000 |

18/24

- +2 G A V T V A W K G D S S P V K A G

 1101 GAGCCGTGAC AGTGGCCTGG AAGGGAGATA GCAGCCCCGT CAAGGCGGGA
 CTCGGCACTG TCACCGGACC TTCCCTCTAT CGTCGGGGCA GTTCCGCCCT
- +2 V E T T T P S K Q S N N K Y A A S 1151 GTGGAGACCA CCACACCCTC CAAACAAAGC AACAACAAGT ACGCGGCCAG CACCTCTGGT GGTGTGGGAG GTTTGTTTCG TTGTTGTTCA TGCGCCGGTC
- +2 S Y L S L T P E Q W K S H R S Y

 1201 CAGCTATCTG AGCCTGACGC CTGAGCAGTG GAAGTCCCAC AGAAGCTACA
 GTCGATAGAC TCGGACTGCG GACTCGTCAC CTTCAGGGTG TCTTCGATGT
 - +2 S C Q V T H E G S T V E K T V A P BbsI
- 1251 GCTGCCAGGT CACGCATGAA GGGAGCACCG TGGAGAAGAC AGTGGCCCCT CGACGGTCCA GTGCGTACTT CCCTCGTGGC ACCTCTTCTG TCACCGGGGA
 - +2 T E C S \*

PmeI

ACAGAATGTT CATAGGGGCC CGTTTAAACC CGCTGATCAG CCTCGACTGT
TGTCTTACAA GTATCCCCGG GCAAATTTGG GCGACTAGTC GGAGCTGACA
pM\_Ig\_REV 100%

GCCTTCTAGT TGCCAGCCAT CTGTTGTTTG CCCCTCCCCC GTGCCTTCCT
CGGAAGATCA ACGGTCGGTA GACAACAAAC GGGGAGGGG CACGGAAGGA
pM\_Ig\_REV 100.0%
========

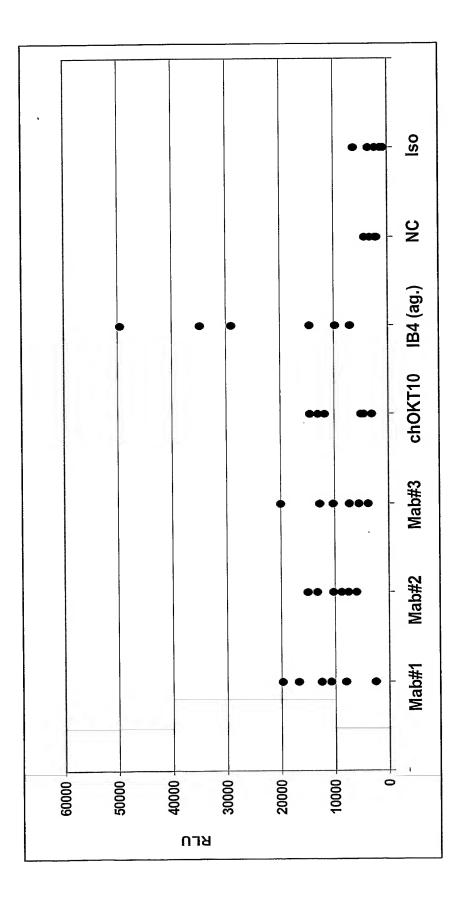
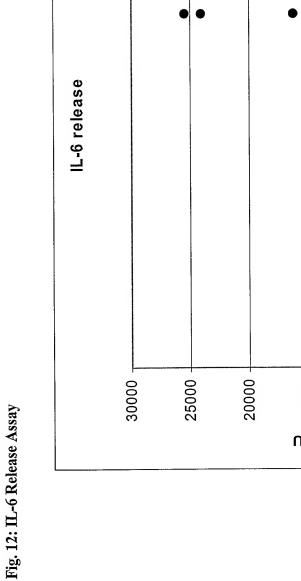


Fig. 11: Proliferation Assay



Medium S Mab#3 chOKT10 IB4 (ag.) Mab#2 Mab#1 15000 10000 5000 0 שרח

Fig. 13: Cytotoxicity towards CD34+/CD38+ progenitor cells

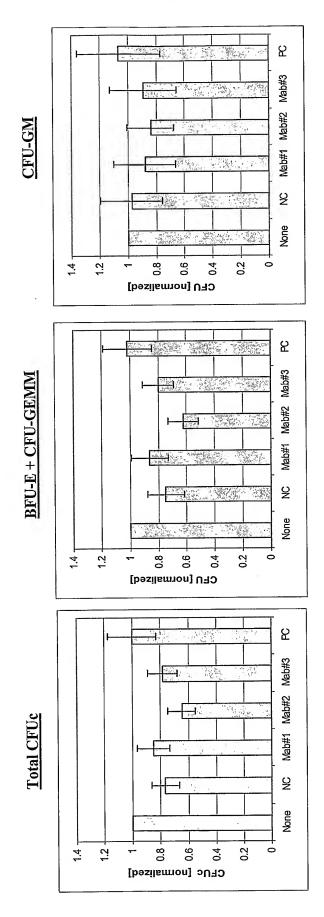


Fig. 14: ADCC with different cell-lines

| | | | Fxpression | Max. s | Max. specific killing [%] in ADGC <sup>a.c.</sup> | ng [%] in A | DCC <sub>a'c</sub> |
|--------------------|---------------------------------|------------------|---------------------|--------|---|-------------|--------------------|
| Cell line | Culture Collection | Origin | IMEIL | Mab#1 | Mab#2 | Mab#3 | PC |
| RPMI 8226 | ATCC CCL-155 | MM | 405.71 | 99 | 28 | 54 | 46 |
| KMS-12-BM | DSMZ ACC551 | MM | 142.29 | 26 | 32 | 30 | 34 |
| NCI-H929 | ECACC95050415 | MM | 45.01 | 89 | 73 | 38 | 54 |
| OPM-2 | DSMZ ACC50 | MM | 37.99 | 9 | 13 | ၁ | 7 |
| U-266 | ECACC85051003 | MM | 26.14 | 17 | 14 | 12 | 16 |
| KMS-11 | Namba et al., 1989 <sup>b</sup> | MM | 26.81 <sup>d</sup> | 22 | 30 | 56 | 28 |
| JVM-13 | DSMZACC19 | CLL | 463.93 | 11 | 20 | 12 | 15 |
| JVM-2 | DSMZACC12 | CLL | 140.84 | 22 | 28 | 10 | 24 |
| CCRF-CEM | ECACC85112105 | ALL | 301.46 | 24 | 29 | 20 | 22 |
| Jurkat | DSMZ ACC282 | ALL | 202.99 | 7 | 8 | 13 | 12 |
| AML-193 | DSMZ ACC549 | AML | 62.69 <sup>d</sup> | 33 | 56 | 39 | 33 |
| OCI-AML5 | DSMZ ACC247 | AML | 207.55 <sup>d</sup> | 20 | 21 | 16 | 26 |
| NB-4 | DSMZ ACC207 | AML | 164.7 <sup>d</sup> | 36 | 38 | 32 | 37 |
| THP-1 | DSMZ ACC16 | AML | 34.41 | 64 | 59 | 38 | 43 |
| HL-60 <sup>d</sup> | DSMZ ACC3 | AML | 18.43 <sup>ն</sup> | 29 | 35 | 58 | 29 |
| Raji | Burkitt's Lymph. | Burkitt's lymph. | .p.u | 53 | 62 | 48 | n.d. |

Fig. 15: ADCC with MM-samples

| Antibodies Parameters: | Mab#1 | Mab#2 | Mab#3 | Dd |
|-----------------------------------|-------------|-------------|-------------|-------------|
| MM samples: EC50 $[nM]^a$: | 0.116-0.202 | 0.006-0.185 | 0.027-0.249 | 0.282-0.356 |
| MM samples: Max spec. killing [%] | 13.1 - 61.6 | 16.2 - 57.9 | 13.6 - 36.0 | 15,5 - 49,5 |

Fig. 16: Treatment of human myeloma xenograft with MOR03080

